

**REMARKS**

This paper is responsive to the Office Action dated November 30, 2006. Entry of the amendments and remarks submitted herein and reconsideration of the claimed subject matter pursuant to 37 CFR §1.112 is respectfully requested.

Claims 77 and 154 have been amended above without prejudice to future prosecution to correct dependency and to delete repetitive language, respectively. No prohibited new matter has been added.

At the outset, Applicants note that application 09/724,922, which is related to the present application, was recently allowed. Applicants respectfully request that the Examiner review prosecution of this allowed application for Office consistency.

Turning now to the Office Action for the subject application, the specification has been objected to because the title was allegedly not descriptive of the invention. The title has been amended above, therefore, this objection may now be withdrawn.

Claim 154 has been objected to as a substantial duplicate of claim 154. Applicants respectfully disagree, since claim 154 recites that the substrate is impermeable. In any case, claim 154 has been amended above to remove repetitive language. Reconsideration and withdrawal of the objection are respectfully requested.

Claim 77 was rejected under 35 U.S.C. §112, second paragraph. Specifically, claim 77 was rejected because it was unclear how a polypeptide as recited in claim 77 can be a nucleic acid as recited in claim 76. Applicants have amended claim 77 to correct the dependency such that claim 77 is now dependent on claim 73. Accordingly, the rejection may now be withdrawn.

Claims 163-172 were rejected under 35 U.S.C. §112, first paragraph for allegedly

containing new matter. According to the Office Action, it is not clear from the disclosure at page 11, lines 14-17, that polymers may be attached to beads. Applicants respectfully traverse the rejection.

Applicants believe that it would be clear to the skilled artisan that polymers can be attached to beads in view of the disclosure at page 11, lines 14-17. Further, this application is a continuation-in-part of U.S. Patent Application No. 07/492,462 (issued as U.S. Patent No. 5,143,854 and incorporated by reference at in the first paragraph of the original specification), which also makes it clear that polymers may be attached to beads (see, for example, the description of a substrate as including particles and spheres at column 11, lines 16-27, and the demonstration of signal capacity at column 26, section D, using particle beads). Similarly, this application is related to U.S. Application No. 07/626,730 (issued as U.S. Patent No. 5,547,839) which was incorporated by reference in the first paragraph of the original specification by attorney reference number and also in the Amendment filed November 28, 2000. This related application also makes it clear that polymers may be attached to beads (see, for example, Figure 4 and the description for Figure 4 at col. 8, lines 31-53, and the description of a suitable substrate at column 10, lines 16-30).

In view of the disclosures discussed above, Applicants respectfully submit that it would be clear to the skilled artisan reading the application as a whole, including all disclosures that are incorporated therein, that polymers may be attached to beads on an array. Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 57-59, 65-67 and 73-75 were rejected under 35 U.S.C. §102(b) as being allegedly anticipated by Shack et al. Applicants respectfully traverse the rejection. As acknowledged in the Office Action, Shack et al. teach epithelial cells located to distinct

locations of a microscope slide. However, since each cell is the same and would express multiple copies of the same polymers on its surface, the substrate would not contain at least 400 diverse polymers per  $\text{cm}^2$ , wherein each diverse polymer has a different sequence as recited in the current claims. Reconsideration and withdrawal of the rejection under 35 U.S.C. §102(b) based on Shack et al. are respectfully requested.

Claims 57, 65, 78, 86, 94, 108, 120, 132 and 144 were rejected under 35 U.S.C. §102(a) as being allegedly anticipated by Southern (WO 89/10977). In addition, claims 57-60, 63-68, 71-76, 78-82, 84-90, 92-98, 100, 101, 108, 113-120, 123-125, 129-132, 135-136, 141-144, 149, 151-152 and 156-162 were rejected under 35 U.S.C. §103(a) as being allegedly obvious over Southern in view of Rushbrooke *et al.* (WO 88/04045). According to the Office Action, Southern teaches a polymer array with a cell size of  $100 \mu\text{m}^2$  which is greater than the instantly claimed polymer density of 10,000 polymers per  $\text{cm}^2$ . Applicants respectfully disagree.

At the outset, Applicants note that all independent claims of the subject application indicate the substrate has at least 400 different polymers per  $\text{cm}^2$ . Southern was also cited in co-owned application 08/897,034, but was withdrawn as failing to teach the claimed densities. For instance, on page 6 of the Amendment filed April 21, 1998 in Serial No. 08/897,034 (now U.S. Patent No. 5,871,928), Applicants asserted:

Southern sets forth a hypothetical case in which 256 X 256 elements would be present in an array that is approximately 256 mm square. Page 24, lines 16-19. Southern provides no indication or suggestion as to how such densities might be achieved. Instead, Southern states that “the narrowest stripe we have laid is 1 mm . . .” Page 23, line 35 to page 24, line 1. Synthesis of a molecule in a 1 mm stripe is a far cry from synthesis of a unique molecule in an area of 1 mm x 1 mm. For example, one unique molecule in a 1 mm stripe on a microscope slide corresponds to 1.3 unique molecules/ $\text{cm}^2$  using the length of the slide (1/1 mm x 76 mm) or 3.85 unique molecules/ $\text{cm}^2$  using the width of the slide (1/1 mm x 26 mm). The latter density is quite close to what Southern

reports as having actually achieved: 72 different polynucleotides in a total surface area of 26 mm x 76 mm (Example 3), or 3.54 polynucleotides/cm<sup>2</sup>. Southern does not remotely show how one might realize the density recited in Applicants' claims.

Further, the crudeness of Southern's techniques were also addressed in the Preliminary Amendment for a related application, a copy of which was also submitted with the above-referenced Amendment in the '034 parent application. As discussed therein (pp. 5-6):

In Example 1, Southern synthesized dT oligomers of different lengths by immersing a microscope slide in a coupling solution at different depths. An automated pen plotter was used in Example 5, but merely to add one base out of 12. In Example 3, Southern offset masks by 3 mm up or down a derivatized slide. The masks were made of rubber tubing having an outer diameter of one mm glued in a U-shape to the surface of a second microscope slide. Such methods are unwieldy at best.

Disturbingly, in Example 3, approximately 1 mm at each edge of a feature is "lost" due to the presence of the rubber tube flattened against the surface on which synthesis takes place. In fact, the highest density actually accomplished is in Example 3 at 72 different polynucleotides in a total surface area of 26 mm x 76 mm (see page 14, lines 32-33), or 3.5 polynucleotides/cm<sup>2</sup>. Even ignoring the lack of unique molecules in each feature, the density of the features reported is merely 4.6 features/cm<sup>2</sup> (90/26 mm x 76 mm). And if one further ignores the large amount of surface area wasted during synthesis and calculates density based upon the sum of the areas of the features as opposed to the total area of the surface on which the features reside, the density is still a paltry 4.8 features/cm<sup>2</sup> (90/[26 mm x 76 mm]-90 mm<sup>2</sup>). Clearly, Southern's methods are interesting, but hardly practical.

Thus, the Office has already determined based on the above arguments during prosecution of co-owned application No. 08/873,034 that Southern does not enable a density of 400 polymers/cm<sup>2</sup> as recited in the instant claims. Accordingly, Southern is not 102(a) prior art.

With regard to the rejection under 35 U.S.C. §103(a), Rushbrooke *et al.* was cited for teaching computer software and a microscope system for inputting fluorescence intensity data

based on photon counts. Rushbrooke *et al.* does not make up for the deficiencies of Southern described above. Therefore, since Southern does not teach polymer arrays as recited in the present and amended claims, it could not have been obvious to make computer program products and software for analyzing such arrays in view of Rushbrooke *et al.*, which does not make up for the deficiencies of the Southern disclosure.

In view of the above amendments and remarks above, reconsideration and withdrawal of the §102(a) rejection based on Southern, and the §103(a) rejection based on Southern and Rushbrooke *et al.*, are respectfully requested.

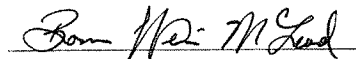
Except for issue fees payable under 37 C.F.R. 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. 1.16 and 1.17 which may be required, including any required extension of time fees, or credit any overpayment to Deposit Account 50-1283. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. 1.136(a)(3).

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